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14. ABSTRACT Five academically qualified students, 3 each from Delaware St. University (DSU) and 2 from Lincoln University, were offered slots in the PCRP program. All accepted. One student withdrew due to personal emergency and was not replaced. Students did 10-week research rotations in addition to attending research seminars and roundtable discussions on the basis of health disparities. This latter topic was not in the initial grant but was received favorably again this year. Students presented research posters in a joint undergraduate research symposium at the end of the summer with almost 200 other students from several summer student research programs. Student presentations and posters were revised through instruction and these were presented at other national meetings (IMPACT and ABCRMS). One student was selected for an oral presentation at IMPACT and won a prominent award at ABCRMS. Graduating students from Lincoln University and Del. St. University are applying to Graduate Schools for post-baccalaureate education. One intends to continue a second year in our PCRP. Two mentors (Ken van Golen and Carlton Cooper) gave 3 lectures at Lincoln University and Delaware State University in 2007. A prominent African-American physician from Johns Hopkins was recruited for a joint talk hosted at UD. Talks will continue in 2008.					
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Introduction:

Due to the extremely low levels of minority faculty and graduate students in the sciences, the DoD Majority Institution (MI) /Historically Black College and University (HBCU) program was intended to foster and promote the interest of minority students in basic science and research by partnering one or more HBCU with a sponsoring MI. In Delaware, this has been accomplished by coordinating student recruitment from Delaware State University and Lincoln University to perform funded summer research in prostate cancer laboratories at the University of Delaware. Our Aims were to 1) offer a 10-week summer research program to five qualified minority students, 2) Offer a summer enrichment program to these students and 3) offer activities and extended research at the participating HBCUs during the following academic year.

Body:

In compliance with Aim 1, and upon the recommendation of the faculty campus coordinators at Delaware State and Lincoln Universities, three students from Lincoln and two students from Delaware State University were chosen for admission into the University of Delaware's training program in Prostate Cancer. One student from Delaware State University, Mary Terese Anangfac, subsequently withdrew at the beginning of the summer to return to her home country on emergency leave. Each student chosen was recognized by the campus coordinator as being academically excellent (3.0 grade point average or above) and motivated to do research. Students in the program participated through "hands-on" research in their designated mentors' laboratories for 10 weeks during the summer. In addition, we implemented a new interdisciplinary research opportunity between Biology and Physics. **Adaire T. Heady**, had two research mentors, Dr. Robert Sikes in Biology and Dr. Michael J. Bonder in Physics. We also had a change in coordinators. Due to serious health problems, Dr. Charles Wilson at Delaware State University was replaced by Cynthia van Golen.

In compliance with Aim 2, students attended weekly seminars related to research <http://www.udel.edu/chem/white/HHMI3/Summer07/S07enrichment.html>., In addition our students attended discussion sessions on the topic of *Healthcare Disparities*. These discussion sessions were not proposed in the grant but were quite successful and popular as judged by a survey that students were required to fill out. Prior to each session students were assigned to read both popular and scientific literature regarding the socio-economic or medical causes of healthcare bias. UD faculty from the Departments of Biological Sciences, Chemistry and Biochemistry and Philosophy led the discussions.

In compliance with Aim 3, four faculty lectures were given during the academic year. Kenneth van Golen gave two lectures, one at DSU and one at Lincoln, and Carlton Cooper one at DSU. Arthur Burnett (MD/PhD), Johns Hopkins School of Medicine, Division of Surgery, Department of Urology gave a special lecture for the students at UD.

Key Research Accomplishments:

The students in this program were expected to make significant progress in research over a 10 week period. Much of this time was spent instructing them in laboratory procedures that included basic liquid handling, safety, and use of technology and equipment required. Despite this, the amount of publishable data that each student collected during this short time is amazing. Additionally, students were instructed to journal their research experience to enhance their level

of comfort of communicating what skills and techniques they learned as well as understanding the research project. At the end of the summer program, each student presented the results of their research at the University's undergraduate research symposium. The symposium was modeled after the Experimental Biology meeting, where posters and talks occurred simultaneously and where there was a plenary lecture by a Howard Hughes Medical Institute investigator <http://www.udel.edu/chem/white/HHMI3/Summer07/S07symposium.html>. The summer symposium taught the students how to communicate their findings to an audience of faculty, postdoctoral students and graduate students through poster presentation. Criticisms at this symposium led to changes in their posters which were presented at national meetings. This was key in providing students feedback and a level of comfort that was obvious at their presentations of results at the IMPaCT meetings held in Atlanta in September 2007. In preparation for national meetings such as ABRCMS, pre-conference meetings were held to coach students on improving their presentation skills as well as networking ability and conference etiquette.

Reportable Outcomes:

*Presentations were made at **both** the IMPaCT meeting (Atlanta, GA, September 2007) and ABRCMS meeting (Austin, Texas; November 2007) (N=6)*

- ♦ Development of Magnetic Nanoparticle Hyperthermia Induced Wound-Healing Assay in Prostate Cancer Cells. **Adaire T. Heady**, Michael J. Bonder, Ph.D., David J. DeGraff, M.S., Robert A. Sikes, Ph.D., George C. Hadjipanayis, Ph.D., Delaware State University, Dover, DE, USA, University of Delaware, Newark, DE, USA (Mentor: Robert Sikes & Michael Bonder)
- ♦ The Roles of RhoG, Rac1, and Rac3 GTPases in PC-3 Human Prostate Cancer Tumor Cell Diapedesis. **Mashariki Jenkins-Kabaila**, Moumita Chatterjee, Kenneth van Golen, Ph.D. Lincoln University, Lincoln University, DE, USA, University of Delaware, Newark, DE, USA. (Kenneth van Golen: Mentor)
- ♦ Adhesion Mediated Chemoresistance of Pc3 Cells to Docetaxel. **Osemeke Edobor**, Freddie Pruitt, Robert Sikes, Kenneth van Golen, Carlton Cooper. Lincoln University, PA, Lincoln University, PA, USA, University of Delaware, Newark, DE, USA. (Mentors: Sikes, van Golen & Cooper)
 - First place poster presentation in cell biology at ABRCMS
 - Oral presentation at ImPACT

Presentations made only at IMPaCT meeting (Atlanta, GA, September 2007)

- ♦ Ion Channel Therapeutics in Prostate Cancer. **Brenda Mogere**, Jennifer Ambrose, and Robert A. Sikes. Lincoln University, PA, Lincoln University, PA, USA, University of Delaware, Newark, DE, USA. (Mentor: Robert Sikes)

Presentation at Lincoln University Undergraduate Research Symposium

- ♦ **Osemeke Edobor**: Second place award Cell Biology

In addition to the aforementioned summer poster presentations, poster session attendance, and poster presentations at national meetings (total of nine posters or talks), each student was asked

recently about their plans for coming year since the programs' research experience is meant to foster an interest in research.

Osemeke Edobor applied for summer research opportunity at Princeton University.

Mashariki Jenkins-Kabaila wants to continue her research at the University with her mentor, Kenneth van Golen.

Adaire T. Heady will not be doing research this summer because she needs to take courses at UD over the summer to complete her dual degree (Physics and Electrical Engineering).

Brenda Mogere is graduating and has applied to graduate and medical schools.

We are currently in the recruiting stage for the upcoming summer program. We have identified the following laboratories as possible placements at the University of Delaware: Dr. Sikes, Dr. Cooper, Dr. Koh, Dr. DeLeon, Dr. van Golen, and Dr. Randall Duncan. To this end we have had student faculty recruiting meetings at Lincoln University with a scheduled meeting at DSU later this month. One of the students, **Mashariki Jenkins-Kabaila**, will be continuing her research as described above. Six new students from Lincoln and one from Delaware State University have been recommended to date. Our application deadline is at the end of February.

Conclusions:

The program seems to be off to an admirable start. For this and last year all nine of our students generated publishable data and five of the nine presented their results at national meetings. We have made changes required to increase communication between faculty involved in research at the HBCUs during the academic year. Coordination of research projects consistent with the capabilities of the HBCU is definitely required to minimize student commuting during the academic year and maximize research productivity at the HBCUs. We have increased the number of minority students applying to graduate schools.

References:

Not Applicable to date.

Appendices:

Abstracts-Used for multiple meetings as described above (4)

Development of Magnetic Nanoparticle Hyperthermia Induced Wound-Healing Assay in Prostate Cancer Cells

Adaire T. Heady, Michael J. Bonder, Ph.D., David J. DeGraff, M.S., Robert A. Sikes, Ph.D., George C. Hadjipanayis, Ph.D., Delaware State University, Dover, DE, USA, University of Delaware, Newark, DE, USA

The use of magnetic nanoparticle (MNP) hyperthermia to an induced wound from Prostate Cancer (PCa) cells, specifically Lymph Node Carcinoma of the Prostate (LNCaP) cells, will exhibit cell migration to that of normal cells. PCa is one of the most common malignancies and remains to be second leading cause of cancer deaths in men in the United States. Although there is no effective, long-term cure for PCa, studies demonstrate that there are advantages in utilizing MNPs for biomedical application with cancer detection and treatment. Iron (Fe) MNPs are manufactured from a chemical synthesis reacting Sodium Borohydride (NaBH_4) in Deionized Water ($\text{DI H}_2\text{O}$) with Iron Chloride (FeCl_2) in Ethanol (EtOH) in a Y-junction reaction tube, which is released into Polyethylene Glycol (PEG) in EtOH. From a prior study, we find that the 1.6-milliliter Y-junction reaction tube has the best results in relation to particle size and temperature. We expose the Fe MNPs to hyperthermia treatments through Heat Introduction. In order to make any progress the FE MNPs must reach temperatures about 50°C , which is the known temperature of cell death. We investigate the suspension of FE MNPs in cell compatible solution and the LNCaP uptake of Fe MNPs. Furthermore, we examine the induced wound-healing assay to acquire information of the migration of the LNCaP cells.

The Roles of RhoG, Rac1, and Rac3 GTPases in PC-3 Human Prostate Cancer Tumor Cell Diapedesis

Mashariki Jenkins-Kabaila, Moumita Chatterjee, Kenneth Van Golen, Ph D.
Lincoln University, Lincoln University, DE, USA,
University of Delaware, Newark, DE, USA.

Based on previous research, the downregulation of the RhoC GTPase in PC-3 human prostate cancer cells derived from bone metastasis leads to increased and sustained levels of Rac GTPase activity. It has been shown that the Rac GTPases are involved in prostate cancer cell migration and invasion particularly through bone marrow endothelial cells. In the current study, we examine the levels of expression, activation, and phenotypic effects of Rac1, Rac3, and RhoG GTPases. The relative and quantitative levels of Rac1, Rac3, and RhoG were compared in PC-3 cells and C3 exotransferase treated PC-3 cells. A Western Blot was performed to show the presence of RhoG in PC-3 cells compared to the presence of RhoG in dnRhoC PC-3 cells. After RhoG was shown to be present, an Evocycler PCR was done to show the relative levels of Rac1, Rac3, and RhoG. Since Rac1 was obviously the larger product a qPCR was done to show exactly how much Rac1 was expressed compared to Rac3 and RhoG. Rac1 was treated with C3 exotransferase its expression became even higher. In the future, it will be compared to siRNA treated cells. A tumor cell diapedesis assay will be done across a monolayer of bone marrow endothelial cells after siRNA treatment of Rac1, Rac3, and RhoG to determine the individual contributions of each GTPase to a cell's invasive capability. We will determine the phenotypic and physiological effects of Rac1, Rac3, and RhoG more closely. We plan to calculate changes in morphology, cell deformation, and binding strength using Atomic Force Microscopy.

Adhesion Mediated Chemoresistance of Pc3 Cells to Docetaxel

Osemeke Edobor, Freddie Pruitt, Robert Sikes, Kenneth van Golen, Carlton Cooper.
Lincoln University, PA, Lincoln University, PA, USA,
University of Delaware, Newark, DE, USA.

Men who develop metastatic prostate cancer (PCa) and fail androgen ablation therapy rely on docetaxel (taxotere) as the next therapy of choice. Unfortunately, patients frequently relapse after developing docetaxel chemo-resistance. Understanding the cellular mechanism that underlies chemo-resistance could improve treatment response for bone metastatic PCa. To determine if type I collagen, which comprises 90% of the bone extracellular matrix (ECM), contributes to chemoresistance, we used an androgen independent bone metastatic PCa cell line, PC3. PC3 cells preferentially activate survival pathways during adhesion to type I collagen. We hypothesize that adhesion of PC3 cells to type I collagen, mediates the chemo-resistance to docetaxel. Our data shows that PC3 cells, when adhered to type I collagen show an increase in p-Akt as compared to PC3 cells on fibronectin and plastic. MTT analysis shows that PC3 cells on type I collagen are more viable in response to increasing concentrations of docetaxel. Western blot analysis shows that type I collagen inhibits the activation of the apoptosis effector, Caspase 7. We believe that Type I collagen protection is mediated by signaling between P13-Kinase inhibitor, LY-294002, was able to negate the protective effects of Type I collagen. In essence, we conclude that adhesion of PCa cells to components of the bone microenvironment may be a critical component of the acquired docetaxel chemoresistance seen in men with bone metastatic PCA.

Funded by: Department of Defense, UDRF

Ion Channel Therapeutics in Prostate Cancer
Brenda Mogere, Jennifer Ambrose, and [Robert A. Sikes](#)
Department of Biological Sciences

Cancer cells have the extraordinary ability to alter their phenotypes and mutate their genotype to attain selective advantage and produce one cell that will survive and colonize at the metastatic site. This is a major cause of treatment failure creating a tremendous hurdle to overcome in designing novel cancer therapeutics. One alternate approach is to examine the interactions between drugs to determine if a previously undiscovered synergy exists. This would enhance tumor cell kill and increase the tolerance of the therapy in the patient by reducing the therapeutic dosage of both drugs. These drugs are chemosensitizers or cooperative chemotherapeutics. Adding drugs at the IC20s helps determine whether synergy with traditional chemotherapy occurs. My research involved obtaining inhibitory concentration curves for different drugs to determine the IC50, IC20 and IC10. Five drugs commonly used to treat prostate cancer Docetaxel, Vinblastine, Cisplatin, Verapamil and Etoposide, were used in this research and two different assays, MTT and crystal violet, were applied to determine cell viability. LNCaP cells were plated at 360,000 cells per 48 well plate followed by treatment with respective drugs for 5 or 7 days and the results were analyzed. To date we have obtained good dose-response curves for Docetaxel that will allow us to calculate the IC20 and begin synergy experiments with sodium channel blockers. Source of Funding: Department of Defense.